

What is claimed is:

1. A method of producing complete Hepatitis A Virus particles comprising the steps of treating an HAV preparation from a cell culture supernatant of an HAV infected cell culture with a nucleic acid degrading agent and a protease, and isolating said purified preparation of complete HAV particles.
2. The method according to claim 1, which further comprises concentrating said cell culture supernatant prior to treating said nucleic acid degrading agent and protease.
3. The method according to claim 2, which comprises concentrating said cell culture supernatant by filtering.
4. The method of claim 1, wherein the nucleic acid degrading agent is an enzyme.
5. The method according to claim 4, wherein the enzyme is a DNase.
6. The method according to claim 1, wherein the protease is a microbial protease.
7. The method according to claim 1, wherein said protease is Pronase or an enzymatically active fraction thereof.
8. The method according to claim 1, wherein said protease is purified *Streptomyces griseus* trypsin.
9. A method according to claim 1, wherein the cell culture is a VERO cell culture.

10. The method according to claim 1, wherein said cells are grown in a serum free or serum and protein free medium.

11. The method according to claim 1, wherein said preparation of purified complete HAV particles is isolated by filtering.

12. The method according to claim 1, wherein said preparation of complete HAV particle has less than about 30 pg contaminating nucleic acid/ IU HAV antigen.

13. The method according to claim 1, wherein said preparation of complete HAV particle has at least about 5000 IU of HAV antigen / mg protein.

14. The method according to claim 1, further comprising a step of treating the preparation of complete HAV particle with a virus inactivating agent.

15. A method of production of a purified Hepatitis A Virus preparation comprising the steps of treating the HAV preparation from the supernatant of an HAV infected cell culture with a nucleic acid degrading agent and a protease, isolating said purified preparation of complete HAV particles and isolating purified mature HAV virions from said preparation complete HAV particle.

16. The method according to claim 15, which comprises concentrating said cell culture supernatant prior to treating said nucleic acid degrading agent and protease.

17. The method according to claim 16, which comprises concentrating said cell culture supernatant by filtering.

18. The method of claim 15, wherein the nucleic acid degrading agent is an enzyme.

19. The method according to claim 15, wherein the protease is a microbial protease.

20. A method according to claim 15, wherein the cell culture is a VERO cell culture.

21. The method according to claim 15, wherein said cells are grown in a serum free or serum and protein free medium.

22. The method according to claim 15, wherein said preparation is substantially free of contaminating proteins from the cells or the cell culture medium.

23. The method according to claim 15, wherein said preparation has less than about 0.5 pg contaminating nucleic acid /IU HAV antigen.

24. The method according to claim 15, comprising a step of treating the purified HAV particles with a virus inactivating agent.

25. The method according to claim 24, wherein treating of purified HAV particles with a virus inactivating agent is performed prior to isolation of mature HAV virions.

26. A method of production of a purified complete HAV particle preparation consisting which consists of purifying complete HAV particles from a cell culture supernatant an HAV infected cells by filtering.

27. The method according to claim 26, comprising further treating said preparation with a virus inactivating agent.

28. A method of production of a purified mature HAV particle preparation which consists of purifying mature HAV particles from a cell culture supernatant of HAV infected cells by filtering and centrifugation.

29. The method according to claim 28 which comprises further treating with a virus inactivating agent.

30. A method of isolating complete HAV particle from a cell-free cell culture supernatant of HAV infected cells comprising the steps of treating the HAV preparation from the supernatant of an HAV infected cell culture with a nucleic acid degrading agent and a protease, and isolating said purified preparation of complete HAV particles.

31. The method according to claim 30, wherein the preparation is free of HAV precursor polypeptide.

32. A method of isolating mature HAV particle from a cell culture supernatant HAV harvest of HAV infected cells comprising the steps of treating the HAV preparation from the supernatant of an HAV infected cell culture with a nucleic acid degrading agent and a protease, isolating said purified preparation of complete HAV, and isolating from said preparation of complete HAV particle a preparation consisting of mature HAV particle.

33. A preparation of complete HAV particle free of HAV precursor polypeptide and contaminating cell or cell culture protein.

34. The preparation according to claim 33, wherein said preparation has less than about 30 pg contaminating nucleic acid / IU HAV antigen.

35. The preparation according to claim 34, wherein said preparation has at least about 5000 IU of HAV antigen / mg protein.

36. The preparation according to claim 33, consisting of inactivated, purified complete HAV particles.

37. A preparation of purified mature HAV particle free of HAV precursor polypeptide and contaminating cell or cell culture protein.

38. The preparation according to claim 37, which is free of HAV provirions.

39. The preparation according to claim 37, wherein said preparation has less than about 0.5 pg contaminating nucleic acid from the cells or the cell culture / IU of HAV antigen.

40. The preparation according to claim 38, consisting of inactivated, purified mature HAV particles.

41. A method for production of HAV vaccine comprising the steps of treating an HAV preparation from the cell culture supernatant of an HAV infected cell culture with a nucleic acid degrading agent and a protease, and isolating said purified preparation of complete HAV particles, and preparing an immunogenic composition comprising a preparation consisting of purified, complete HAV virions.

42. A method for the production of an HAV vaccine comprising the steps of treating the HAV preparation from the supernatant of an HAV infected cell culture

with a nucleic acid degrading agent and a protease, isolating said purified preparation of complete HAV particles and isolating purified mature HAV virions from said preparation complete HAV particle, and preparing an immunogenic composition comprising a preparation consisting of purified, mature HAV virions.

43. The method according to claim 42, wherein the vaccine is substantially free of contaminating proteins from the cell culture.

44. A method for production of an inactivated HAV vaccine comprising the steps of treating the HAV preparation from the supernatant of an HAV infected cell culture with a nucleic acid degrading agent and a protease, isolating said purified preparation of complete HAV particles and isolating purified mature HAV virions from said preparation complete HAV particle, and preparing an immunogenic composition comprising a preparation, wherein the HAV preparation is treated with an inactivation agent prior or after isolating of mature HAV virion particle.

45. AN HAV vaccine comprising an host protective amount of a mature HAV particle preparation according to claim 37.

46. A vaccine according to claim 45, wherein said preparation is free of HAV precursor polypeptide and HAV provirions.

47. The vaccine according to claim 45, wherein said host protective dose is less than about 25 IU of HAV antigen / dose:

48. The vaccine according to claim 45, wherein said host protective dose is between about 10 and about 25 IU of HAV antigen / dose.

49. The vaccine according to claim 45, comprising an immune stimulating agent.

50. The vaccine according to claim 45, further comprising Hepatitis B virus antigen.

51. The vaccine according to claim 45, further comprising an antigen from a viral or bacterial pathogen.

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